Topic 1. Building Blocks of Living Systems

TOPICS
- basic microbiology - cells
- cellular composition
- water
- lipids
- carbohydrates
- nucleic acids
- proteins
- information flow
- cellular stoichiometry

Cells – the basic organizational unit of life

There are entire courses devoted to biochemistry and biophysics, and even to specialized subsets of these fields, so we will only scratch the surface of this vast area of science. Our goal is to become familiar with the categories of biomolecules that are responsible for the structure and basic function of cells.

It was not until 1838 that the concept of the cell as a basic building block of living organisms emerged, when Schleiden and Schwann proposed the *cell theory*. This theory held that all living systems are composed of cells and their products. This idea allows us to "deconstruct" living systems – to think about the structure and function of individual cells, and then to think about how the activities of cells are coordinated in tissues, organs and organisms. Some aspects of cell structure and function are universal, but certainly not all cells are alike. Cells of different species are different, and different cells within multicellular organisms are different. (This is called "differentiation.")

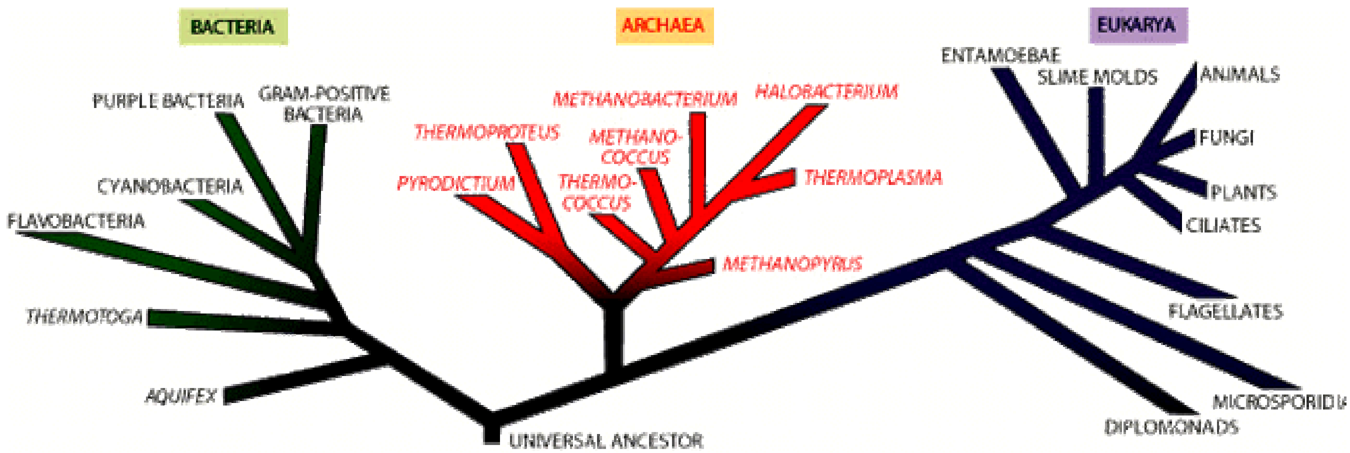
First, let's discuss length scales and the basic structure of cells.

typical molecule dimensions: ~ 1 nm
cell membrane thickness: ~ 5-10 nm
resolution of the light microscope: ~ 0.5 μm
radius of typical cells: ~ 1 – 20 μm
radius of giant amoeba: ~ 100 μm
height of human: ~ 1.8 m

Procaryotes and Eucaryotes
2 generic types of cellular organization distinguished by size and internal organization

Pro karyon = before nucleus
Eu karyon = true nucleus

The Three Domains:



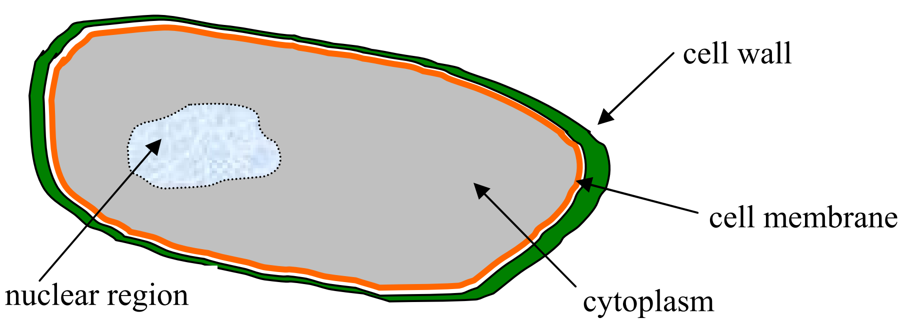
Prokaryotes Eucaryotes

http://fig.cox.miami.edu/~cmallery/150/proceuc/3domainsfig.gif

Procaryotic cells do not contain a membrane-enclosed nucleus. They are relatively small and “simple” cells. They are usually found alone, not associated with other cells. In other words, they are single-cell organisms. Not all single cell organisms are prokaryotes though. Procaryotes include bacteria and algae.

Procaryotes typically measure 0.5 to 3 μm and have a volume ~ 10^{-12} mL, about 50 to 80% of which is water. They grow rapidly, typically doubling in size, mass and number in ~ 20 min, and they are found in a wide variety of environments.

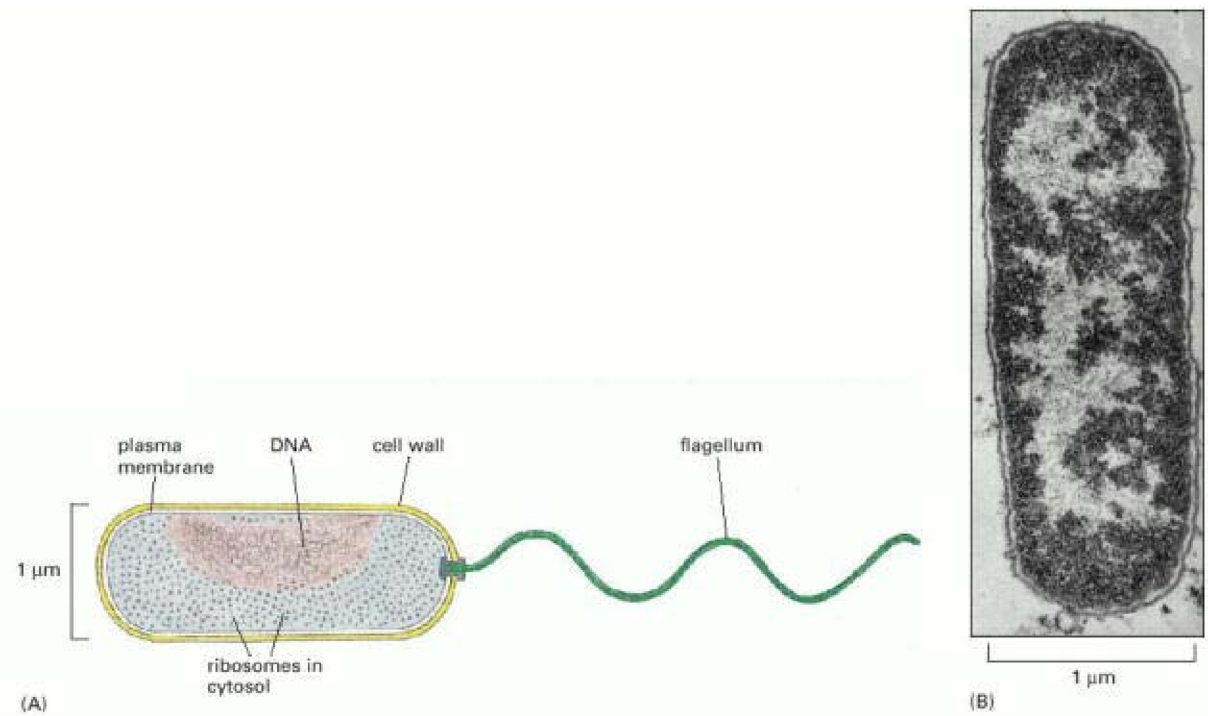
The basic features of the procaryotic cell are:



The cell is surrounded by a rigid *cell wall* that is about 20 nm thick that lends structural integrity to the cell.

Immediately inside the cell wall is the *cell membrane* or *plasma membrane* that is about 7 nm thick. This membrane is common to all cells and plays the important role of determining which types of molecules can enter or leave a cell.

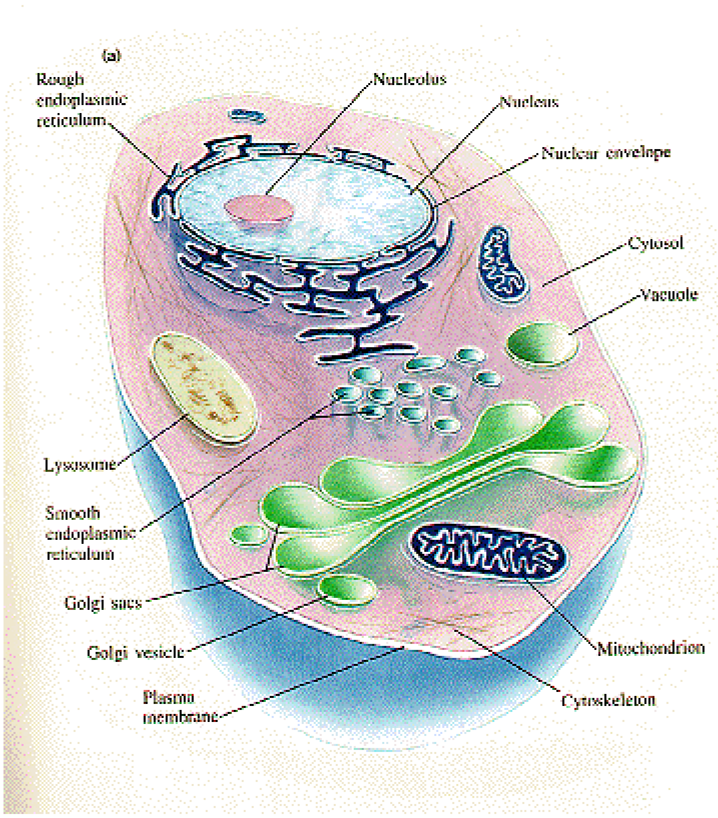
The fluid interior of the cell is the *cytoplasm,* which contains the *nuclear region*, an ill defined region that is the "control center" for most cellular function. In prokaryotes, there is no membrane around the nuclear region. Other items to be found in the cytoplasm include *ribosomes* that produce proteins and *storage granules*.



The structure of a bacterium. (A) The bacterium *Vibrio cholerae,* showing its simple internal organization. Like many other species, *Vibrio* has a helical appendage at one end—a flagellum—that rotates as a propeller to drive the cell forward. (B) An electron micrograph of a longitudinal section through the widely studied bacterium *Escherichia coli (E. coli)*. This is related to *Vibrio* but lacks a flagellum. The cell's DNA is concentrated in the lightly stained region. (B, courtesy of E. Kellenberger.)
http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=mboc4.figgrp.37

Eucaryotes include all other cell types. These are most generally defined as cells that possess a membrane-enclosed nucleus. Eucaryotic cells, typically about 5 to 20 µm, are larger than most prokaryotes. All cells of "higher organisms" are eukaryotes. Eucaryotes often (but not always) live in close association with other cells to form multicellular organisms. Cells of multicellular organisms can be specialized, so that not every individual cell needs to be able to carry out all of the functions needed for the organisms to survive.

The internal structure of eucaryotes is considerably more complex than procaryotes. They are more organized spatially.

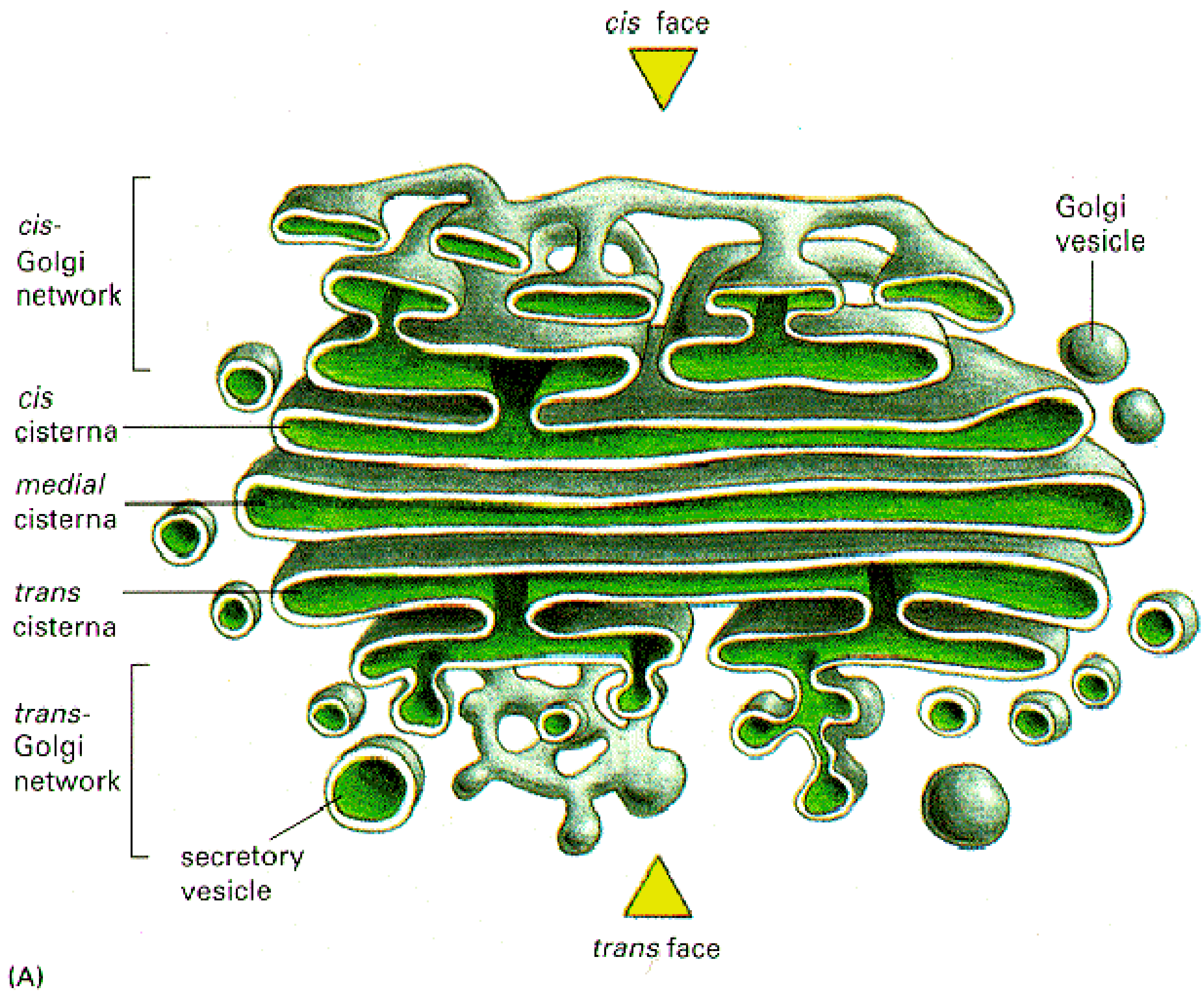


http://ridge.icu.ac.jp/gen-ed/cell-lect-gifs/03-euc-cell-animal.GIF

This is a schematic illustration of an animal cell (animals are eucaryotes). We see the *plasma membrane*, which is similar both in terms of structure and function to the plasma membrane of procaryotes. The fluid inside the cell membrane is the cytoplasm (or cytosol), just as in procaryotes. The *mitochondrion* is a membranous structure responsible for utililizing oxygen to liberate energy from nutrients. The *endoplasmic reticulum* (ER) is another membranous structure that traverses large distances within the cell. Its walls are dotted with *ribosomes* that manufacture proteins. The ER is closely associated with the *nucleus*, where the DNA that encodes the proteins being manufactured in the ER is stored. The *Golgi apparatus* packages and releases cell products, such as hormones, to the outside of the cell.

All of these internal, membrane-enclosed structures are called *organelles* – a sub-cellular part that has a distinct metabolic function. They divide up the many cellular functions into efficient, specialized entities.

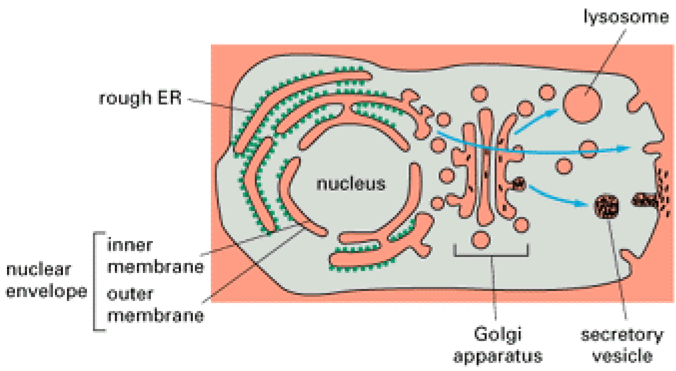
Notice how complex these structures are:



http://ridge.icu.ac.jp/gen-ed/cell-lect-gifs/14golgi-details.GIF

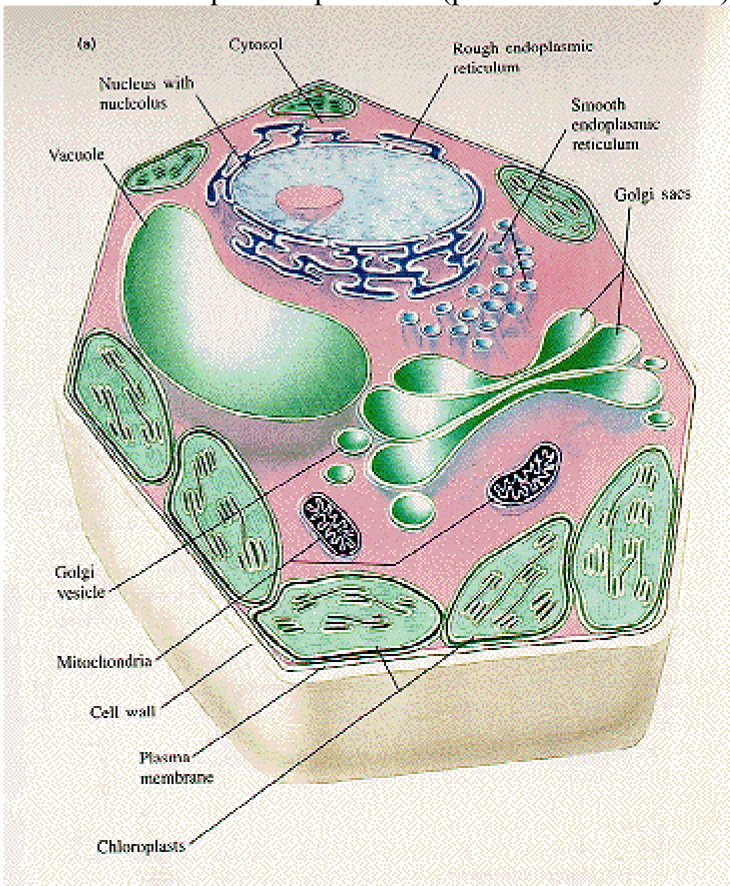
The function of the Golgi apparatus illustrates how the activities of different organelles are highly orchestrated, as illustrated below.

Molecular Biology of the Cell, 3rd edn. ➔Part III. Internal Organization of the Cell ➔**Chapter 12. Intracellular Compartments and Protein Sorting** ➔The Compartmentalization of Higher Cells



Topological relationships between compartments in a eucaryotic cell. Topologically equivalent spaces are shown in *red*. In principle, cycles of vesicle budding and fusion permit any lumen to communicate with any other and with the cell exterior. The *blue arrows* indicate the outward direction of vesicle traffic from the ER to Golgi apparatus to plasma membrane (or lysosomes), and the *black dots* represent protein molecules that are secreted by the cell. Some organelles, most notably mitochondria and (in plant cells) chloroplasts, however, do not take part in this vesicular communication and so are isolated from the traffic between organelles shown here. http://www.ncbi.nlm.nih.gov/books/bv.fcgi?call=bv.View..ShowSection&rid=cell.figgrp.2837

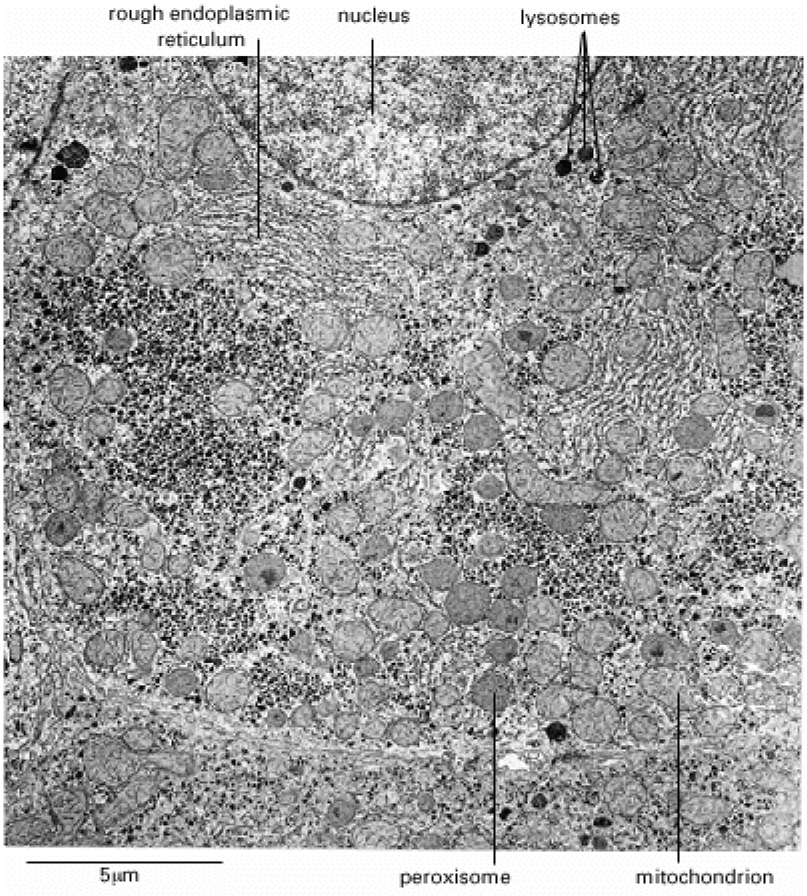
Here is an example of a plant cell (plants are eucaryotes).



http://ridge.icu.ac.jp/gen-ed/cell-lect-gifs/04-eucaryote-plant-cell.GIF

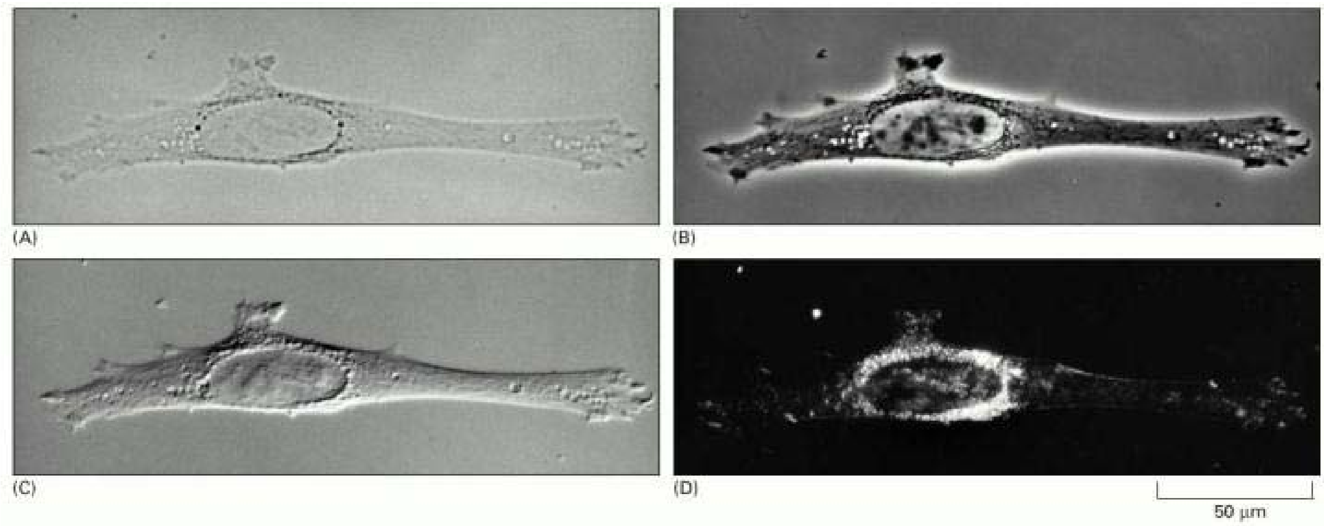
Notice that many features of the plant cell are similar to animal cells. Outside the cell membrane, plant cells have a rigid cell wall. The *chloroplasts* contain the chlorophyll that is the molecule responsible for capturing the energy of the sun and converting it to chemically usable energy.

These beautiful, clear drawings are based mostly on different types of light microscopy and electron microscopy. Here is what the biologist actually "sees" with the transmission electron micrograph:



Electron micrograph of part of a liver cell seen in cross-section. Examples of most of the major intracellular compartments are indicated. (Courtesy of Daniel S. Friend.)
http://www.ncbi.nlm.nih.gov/books/bv.fcgi?call=bv.View..ShowSection&rid=cell.figgrp.2834

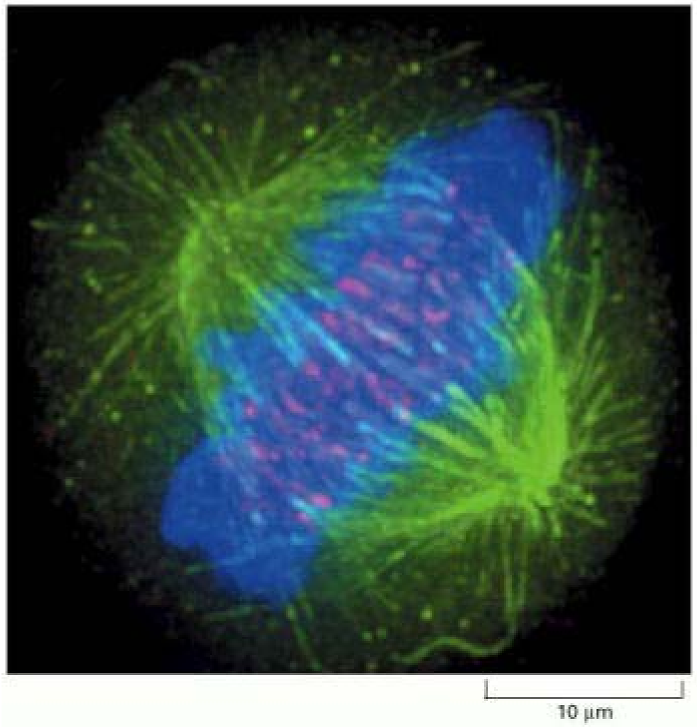
Here are cells imaged by light microscopy
Molecular Biology of the Cell ➔**III. Methods** ➔9. Visualizing Cells ➔Looking at the Structure of Cells in the Microscope



Four types of light microscopy. Four images are shown of the same fibroblast cell in culture. All four types of images can be obtained with most modern microscopes by interchanging optical components. (A) Bright-field microscopy. (B) Phase-contrast microscopy. (C) Nomarski differential-interference-contrast microscopy. (D) Dark-field microscopy. http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=mboc4.figgrp.1729

Using fluorescent dyes and fluorescence microscopy, it is possible to see where different types of molecules localize inside cell:

Molecular Biology of the Cell ➔**III. Methods** ➔9. Visualizing Cells ➔Looking at the Structure of Cells in the Microscope



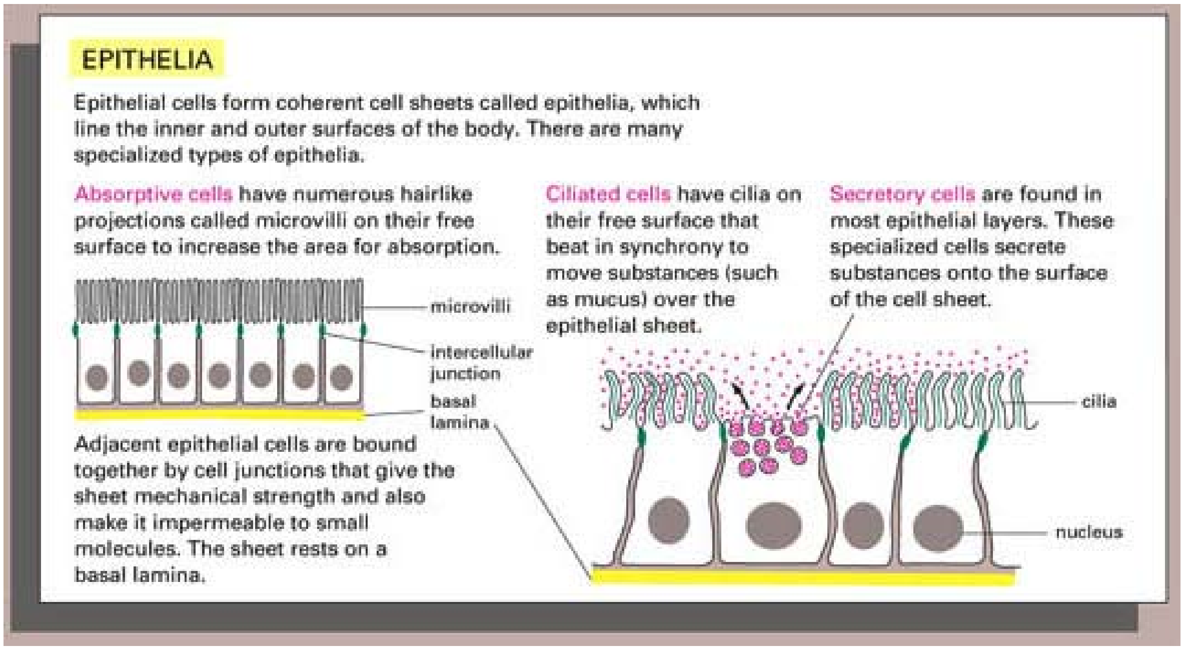
Multiple-fluorescent-probe microscopy. In this composite micrograph of a cell in mitosis, three different fluorescent probes have been used to stain three different cellular components. The spindle microtubules are revealed with a *green* fluorescent antibody, centromeres with a *red* fluorescent antibody and the DNA of the condensed chromosomes with the *blue* fluorescent dye DAPI. (Courtesy of Kevin F. Sullivan.)
http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=mboc4.figgrp.1740

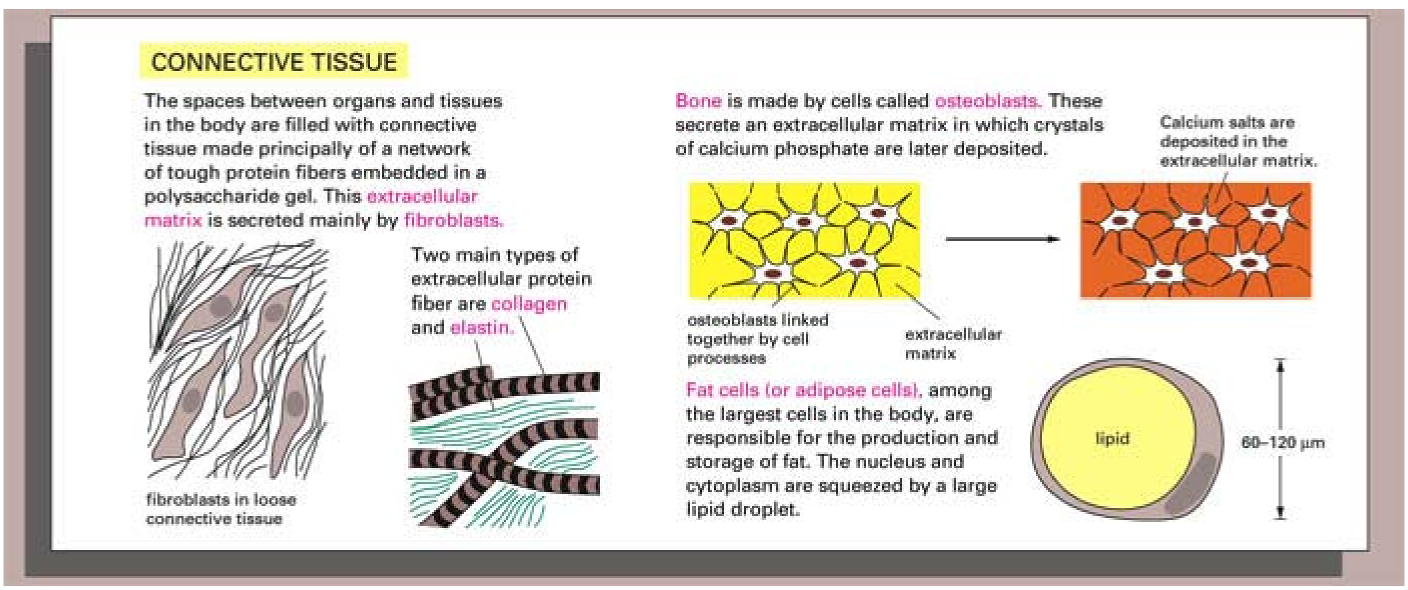
7 Major CHARACTERISTIC of EUCARYOTES:
http://fig.cox.miami.edu/~cmallery/150/proceuc/proceuc.htm

- nucleus - single greatest step in evolution of higher animals
  - genes in "chromosomes" [colored bodies... made of DNA + protein]
  - contains more DNA (1,000x more) than procaryotes
- presence of organelles- significant internal compartmentalization of function
- presence of flexible cell walls (allows phagocytosis)
- presence of cytoskeleton (provides framework to be larger)
- reproduce sexually
- usually larger - cell volume 10X > than bacteria - size 5.0 to 20 μm diameter
- extensive internal membranes

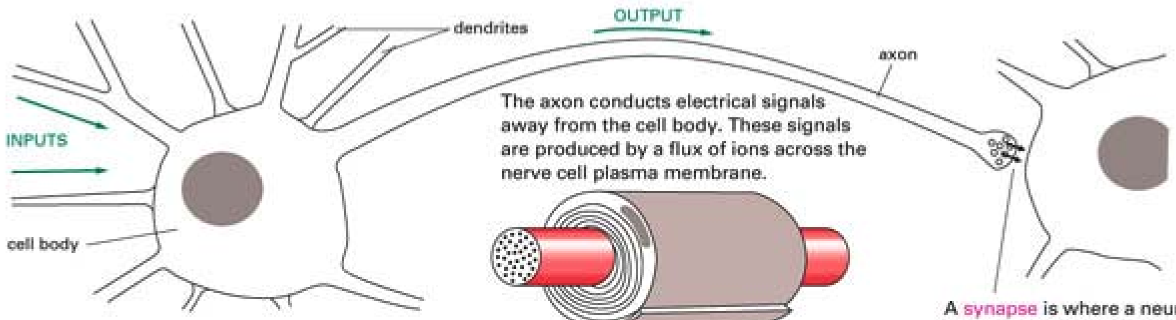
Major types of differentiated mammalian cells
http://www.accessexcellence.org/RC/VL/GG/mammal_Types_1.html

Over 200 cell types in human body used to make up different tissues; most tissues made up of more than one cell type.





NERVOUS TISSUE



Nerve cells, or neurons, are specialized for communication. The brain and spinal cord, for example, are composed of a network of neurons among supporting glial cells.

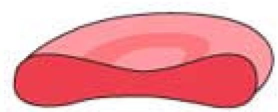
Specialized glial cells wrap around an axon to form a multilayered membrane sheath.

A synapse is where a neuron forms a specialized junction with another neuron (or with a muscle cell). At synapses, signals pass from one neuron to another (or from a neuron to a muscle cell).

BLOOD

Erythrocytes (red blood cells) are very small cells, and in mammals have no nucleus or internal membranes. When mature they are stuffed full of the oxygen-binding protein hemoglobin.

1 cm^3 of blood contains 5 billion erythrocytes

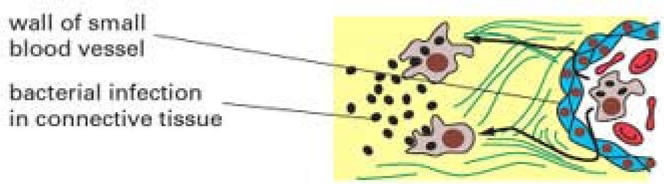


their normal shape is a biconcave disc

Leucocytes (white blood cells) protect against infections. Blood contains about one leucocyte for every 100 red blood cells. Although leucocytes travel in the circulation, they can pass through the walls of blood vessels to do their work in the surrounding tissues. There are several different kinds, including

lymphocytes—responsible for immune responses such as the production of antibodies.

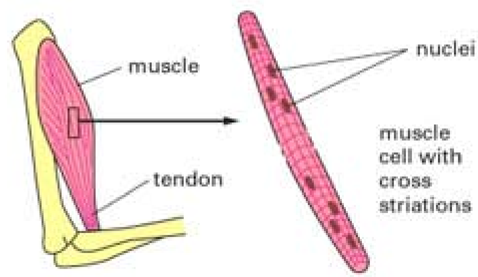
macrophages and neutrophils—move to sites of infection, where they ingest bacteria and debris.



MUSCLE

Muscle cells produce mechanical force by their contraction. In vertebrates there are three main types:

skeletal muscle—this moves joints by its strong and rapid contraction. Each muscle is a bundle of muscle fibers, each of which is an enormous multinucleated cell.

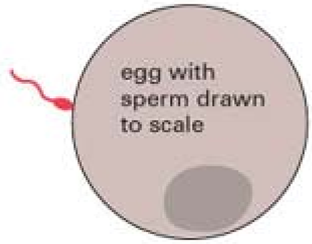


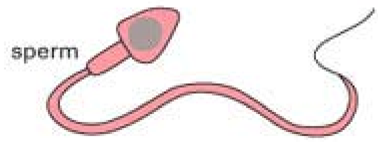
smooth muscle—present in digestive tract, bladder, arteries, and veins. It is composed of thin elongated cells (not striated), each of which has one nucleus.

cardiac muscle—intermediate in character between skeletal and smooth muscle. It produces the heart beat. Adjacent cells are linked by electrically conducting junctions that cause the cells to contract in synchrony.

GERM CELLS

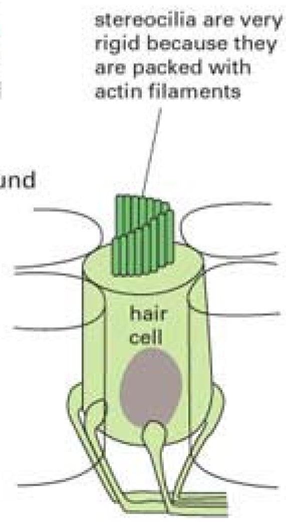
Both sperm and egg are *haploid,* that is, they carry only one set of chromosomes. A sperm from the male fuses with an egg from the female, which then forms a new diploid organism by successive cell divisions.

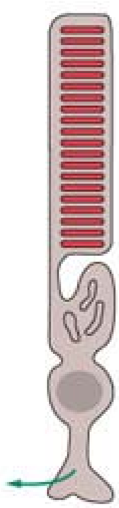




SENSORY CELLS

Among the most strikingly specialized cells in the vertebrate body are those that detect external stimuli. Hair cells of the inner ear are primary detectors of sound. They are modified epithelial cells that carry special microvilli (stereocilia) on their surface. The movement of these in response to sound vibrations causes an electrical signal to pass to the brain.





Rod cells in the retina of the eye are specialized to respond to light. The photosensitive region contains many membranous discs (*red*) in whose membranes the light-sensitive pigment rhodopsin is embedded. Light evokes an electrical signal (*green arrow*), which is transmitted to nerve cells in the eye, which relay the signal to the brain.

Biotechnically-important Cell Types

Bacteria

Production of recombinant proteins, genetic material, vinegar, waste treatment, bioremediation, lactic acid, xanthan gum

Yeasts

Alcohol, glycerol, single cell protein for animal & Aussie feed (think Vegemite), Baker's yeast, recombinant protein production

Molds

Antibiotics, organic acids, enzymes

Archea

Enzymes

Algae

Food and food supplements (carrageenan), filter aids (diatoms)

Protozoa

Waste treatment

Animal cells

Recombinant proteins, engineered tissues

Plant cells

Perfumes, dyes, medicines, opiates, recombinant proteins

Insect cells

Recombinant proteins, viruses

Cellular Composition

Cellular Constituents

Elemental Composition

On a dry basis, for E. coli

element	% dry weight
C	50
O	20
N	14
H	8
P	3
S	1
K	1
Na	1
Ca	0.5
Mg	0.5
Cl	0.5
Fe	0.2
others	~0.3
	100%

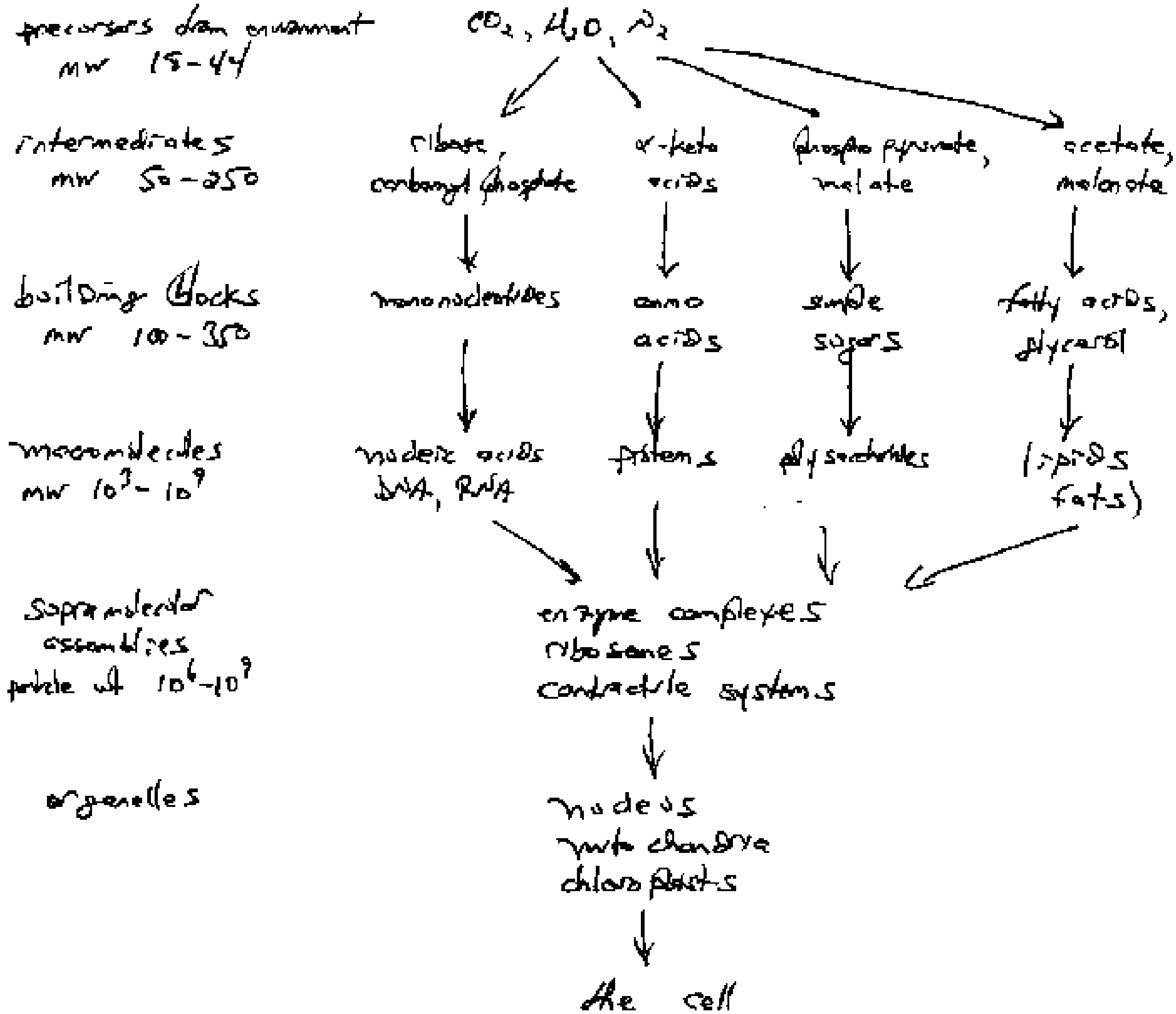
recall, cells have 50-80% H_2O with ~70% typical

if we were to include H_2O, H & O contents would increase dramatically

e.g. if E. coli is 20% by weight O on a dry basis, what is wt % O on wet basis assuming 70% H_2O content?

Example: E. coli dry versus wet basis

Molecular Composition
complexity and organization



On a wet basis, for E. coli in exponential growth

Component	wt%	$\langle MW \rangle$	approx #/cell	approx # of diff types
H_2O	70	18	4×10^{10}	1
inorganic ions	1	40	2.5×10^{8}	20
carbohydrates + precursors	3	150	2×10^{8}	200
amino acids + precursors	0.4	120	3×10^{7}	100
nucleotides + precursors	0.4	300	1.2×10^{7}	200
lipids + precursors	2	750	2.5×10^{7}	50
other small molecules	0.2	150	1.5×10^{7}	200
proteins	15	40,000	10^{6}	2000 – 3000
nucleic acids DNA	1	2.5×10^{9}	4	1
RNA	6			
16S rRNA		500,000	3×10^{4}	1
23S rRNA		1,000,000	3×10^{4}	1
tRNA		25,000	4×10^{5}	40
mRNA		1,000,000	10^{3}	1000

Example: compare composition of oatmeal versus dried *E. coli*….

Building Blocks - Biomolecules

1. **Water.** Although we do not often think of water (H_2O) as a biomolecule, the function of any biomolecule really hinges on the fact that these molecules are designed to work in water. Most often, the biological activity of any biomolecule is severely altered, if not lost altogether, when water is removed from the system.

What makes water unique is its extremely large polarity. The oxygen acquires a partial negative charge, and the hydrogens acquire a partial negative charge, making water a "polar molecule."

Its high polarity allows it to surround ("solvate") ions and stabilize them. This makes salts soluble in water, whereas most salts are not soluble in nonpolar solvents like hexane.

For our purposes, we will generally classify molecules as either ionic or nonionic, depending on whether or not they can dissociate into ions in water, and as either *hydrophilic* (water-soluble) or *hydrophobic* (insoluble in water).

Hydrophilic molecules tend to be ionic or polar nonionic molecules. One clue is to look for one or more OH groups, COOH groups or NH_3 groups.

Hydrophobic molecules tend to be nonpolar and nonionic. Look for molecules that are mostly made up of CH_3 or CH_2 groups.

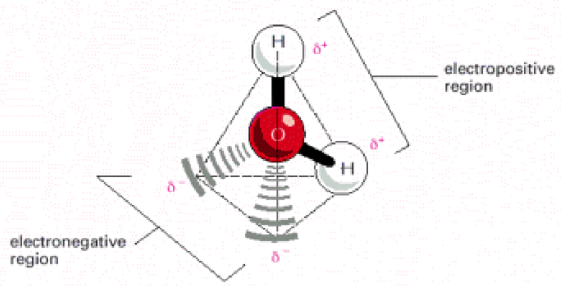
Many important biomolecules are *amphiphilic*, meaning part of the molecule is hydrophilic and part of the molecule is hydrophobic. Amphiphilicity plays a major reole in determining the structure and function of biomolecules. It all has to do with how the molecules respond to water – either to seek out water or to avoid water.

The unique properties of water are summarized here:

Water and Its Influence on the Behavior of Biological Molecules

WATER

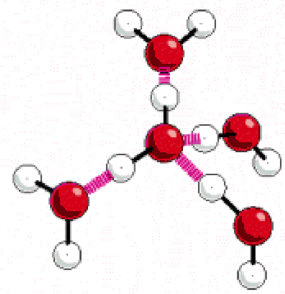
Two atoms, connected by a covalent bond, may exert different attractions for the electrons of the bond. In such cases the bond is polar, with one end slightly negatively charged (δ−) and the other slightly positively charged (δ+).



Although a water molecule has an overall neutral charge (having the same number of electrons and protons), the electrons are asymmetrically distributed, which makes the molecule polar. The oxygen nucleus draws electrons away from the hydrogen nuclei, leaving these nuclei with a small net positive charge. The excess of electron density on the oxygen atom creates weakly negative regions at the other two corners of an imaginary tetrahedron.

WATER STRUCTURE

Molecules of water join together transiently in a hydrogen-bonded lattice. Even at 37°C, 15% of the water molecules are joined to four others in a short-lived assembly known as a "flickering cluster."

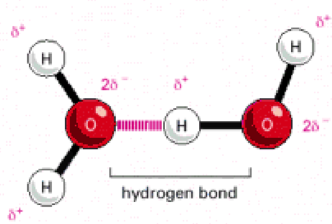


The cohesive nature of water is responsible for many of its unusual properties, such as high surface tension, specific heat, and heat of vaporization.

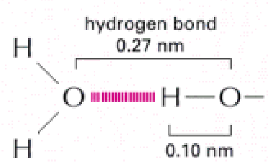
HYDROGEN BONDS

Because they are polarized, two adjacent H_2O molecules can form a linkage known as a hydrogen bond. Hydrogen bonds have only about 1/20 the strength of a covalent bond.

Hydrogen bonds are strongest when the three atoms lie in a straight line.

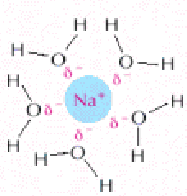


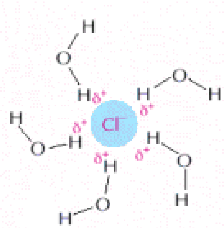
bond lengths



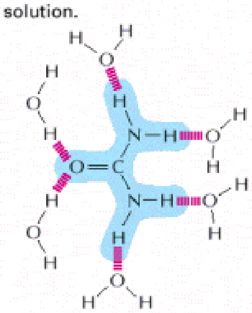
HYDROPHILIC MOLECULES

Substances that dissolve readily in water are termed hydrophilic. They are composed of ions or polar molecules that attract water molecules through electrical charge effects. Water molecules surround each ion or polar molecule on the surface of a solid substance and carry it into solution.





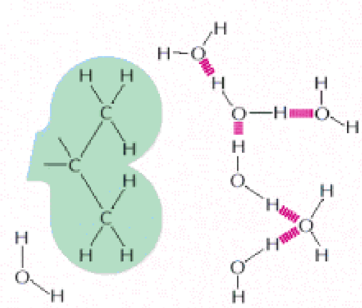
Ionic substances such as sodium chloride dissolve because water molecules are attracted to the positive (Na^+) or negative (Cl^-) charge of each ion.



Polar substances such as urea dissolve because their molecules form hydrogen bonds with the surrounding water molecules.

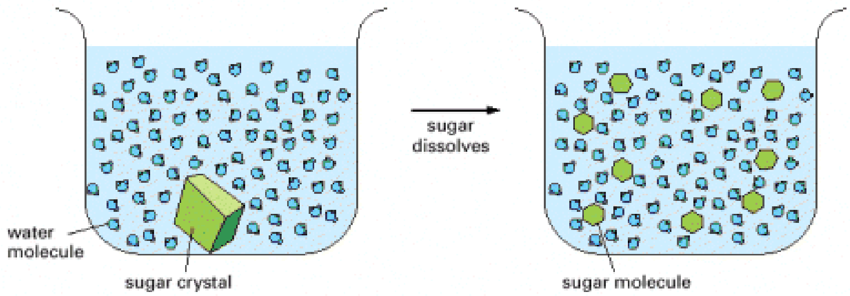
HYDROPHOBIC MOLECULES

Molecules that contain a preponderance of nonpolar bonds are usually insoluble in water and are termed hydrophobic. This is true, especially, of hydrocarbons, which contain many C–H bonds. Water molecules are not attracted to such molecules and so have little tendency to surround them and carry them into solution.



WATER AS A SOLVENT

Many substances, such as household sugar, dissolve in water. That is, their molecules separate from each other, each becoming surrounded by water molecules.



When a substance dissolves in a liquid, the mixture is termed a solution. The dissolved substance (in this case sugar) is the solute, and the liquid that does the dissolving (in this case water) is the solvent. Water is an excellent solvent for many substances because of its polar bonds.

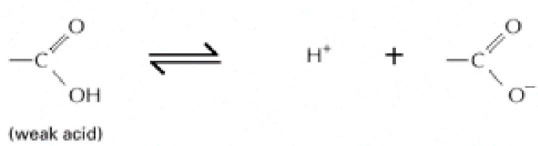
ACIDS

Substances that release hydrogen ions into solution are called acids.

$HCl \longrightarrow H^+ + Cl^-$

hydrochloric acid (strong acid) — hydrogen ion — chloride ion

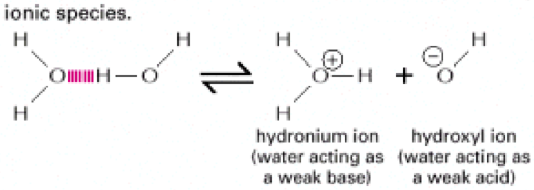
Many of the acids important in the cell are only partially dissociated, and they are therefore weak acids—for example, the carboxyl group (–COOH), which dissociates to give a hydrogen ion in solution



Note that this is a reversible reaction.

HYDROGEN ION EXCHANGE

Positively charged hydrogen ions (H^+) can spontaneously move from one water molecule to another, thereby creating two ionic species.



often written as: $H_2O \rightleftharpoons H^+ + OH^-$

hydrogen ion — hydroxyl ion

Since the process is rapidly reversible, hydrogen ions are continually shuttling between water molecules. Pure water contains a steady-state concentration of hydrogen ions and hydroxyl ions (both 10^{-7} M).

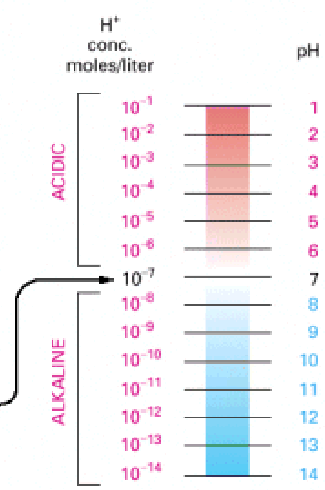
pH

The acidity of a solution is defined by the concentration of H^+ ions it possesses. For convenience we use the pH scale, where

$pH = -\log_{10}[H^+]$

For pure water

$[H^+] = 10^{-7}$ moles/liter



BASES

Substances that reduce the number of hydrogen ions in solution are called bases. Some bases, such as ammonia, combine directly with hydrogen ions.

$NH_3 + H^+ \longrightarrow NH_4^+$

ammonia — hydrogen ion — ammonium ion

Other bases, such as sodium hydroxide, reduce the number of H^+ ions indirectly, by making OH^- ions that then combine directly with H^+ ions to make H_2O.

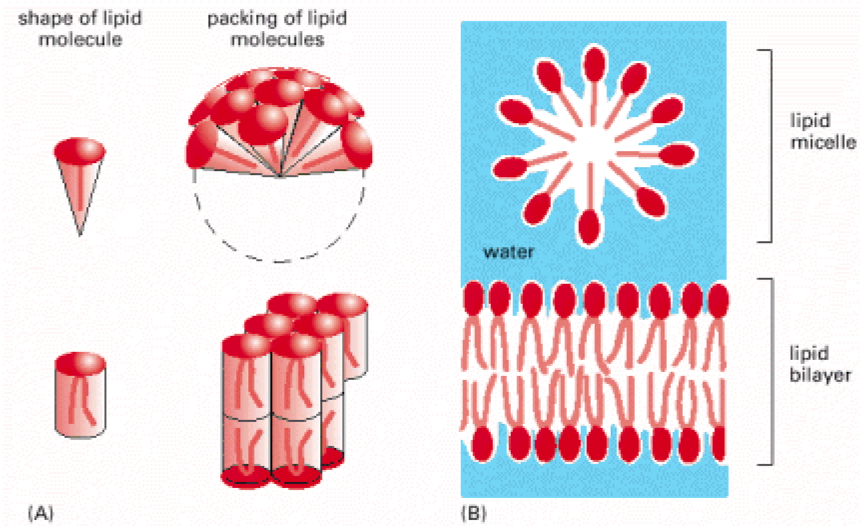
$NaOH \longrightarrow Na^+ + OH^-$

sodium hydroxide (strong base) — sodium ion — hydroxyl ion

Many bases found in cells are partially dissociated and are termed weak bases. This is true of compounds that contain an amino group ($-NH_2$), which has a weak tendency to reversibly accept an H^+ ion from water, increasing the quantity of free OH^- ions.

$-NH_2 + H^+ \rightleftharpoons -NH_3^+$

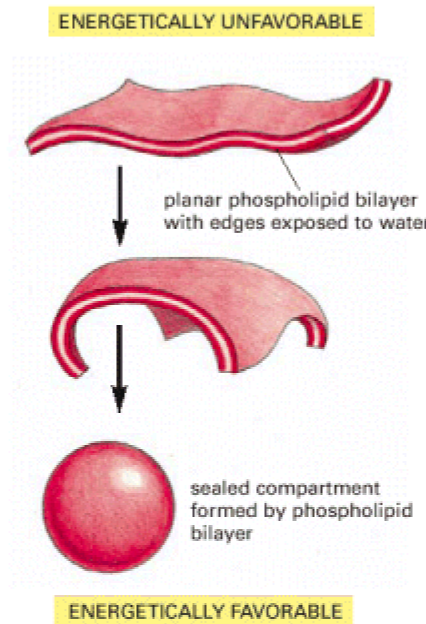
2. **Lipids.** In animal cells, approximately 50% of the molecules in cell membranes are lipids. (Most of the rest are proteins.) Lipids are excellent examples of amphiphilic molecules. They are described as having a hydrophilic *headgroup* and one or more hydrophobic *tails*. The key characteristic of lipids is that they spontaneously *self-assemble* when placed in water. For biological purposes, the *bilayer* is the most important type of self-assembled lipid structure because the basic structural element of cell membranes is the lipid bilayer.



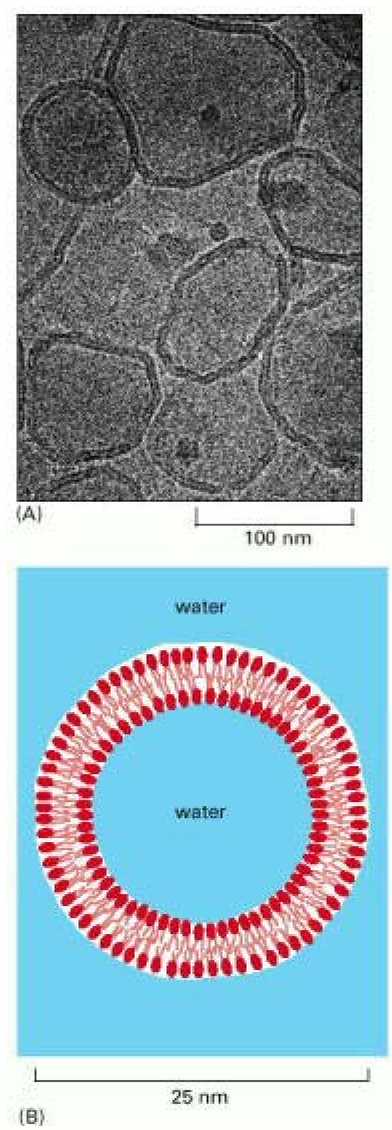
Packing arrangements of lipid molecules in an aqueous environment. (A) Wedge-shaped lipid molecules *(above)* form micelles, whereas cylinder-shaped phospholipid molecules *(below)* form bilayers. (B) A lipid micelle and a lipid bilayer seen in cross section. Lipid molecules spontaneously form one or other of these structures in water, depending on their shape.
http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=mboc4.figgrp.1868

Lipid bilayers spontaneously close upon themselves to form spherical *vesicles* (or "liposomes"). This provides the basic structure of the cell. (To understand why this happens, bioengineers should study physical chemistry and thermodynamics.)

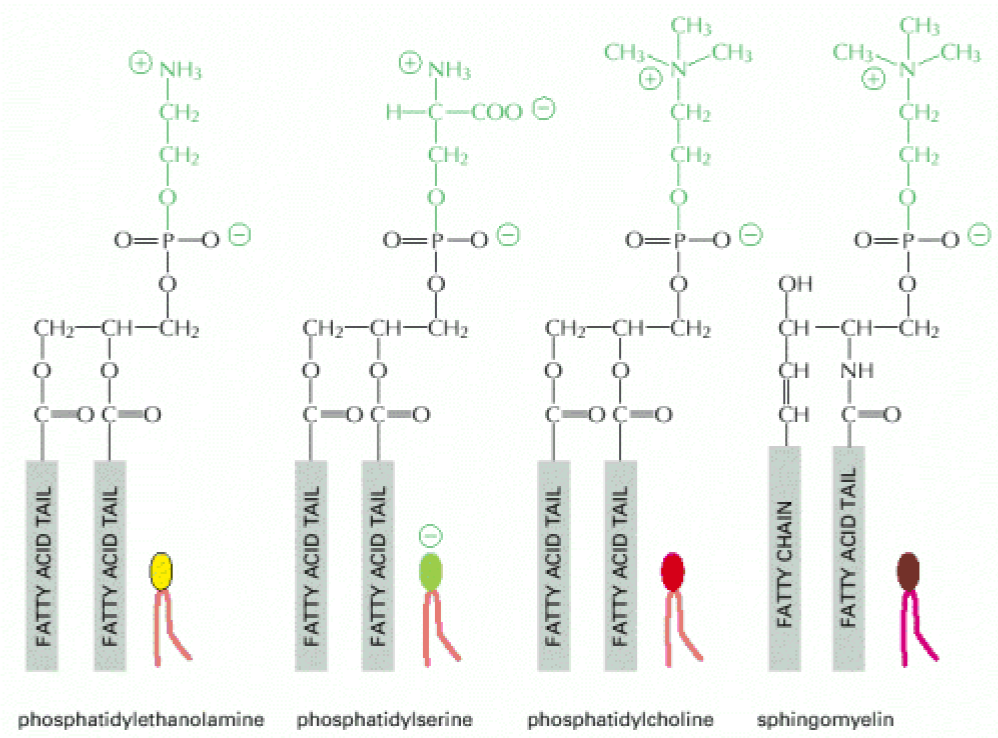
The spontaneous closure of a phospholipid bilayer to form a sealed compartment. The closed structure is stable because it avoids the exposure of the hydrophobic hydrocarbon tails to water, which would be energetically unfavorable.
http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=mboc4.figgrp.1869



Liposomes.
http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=mboc4.figgrp.1871



Here are the chemical structures of the most common types of lipids.

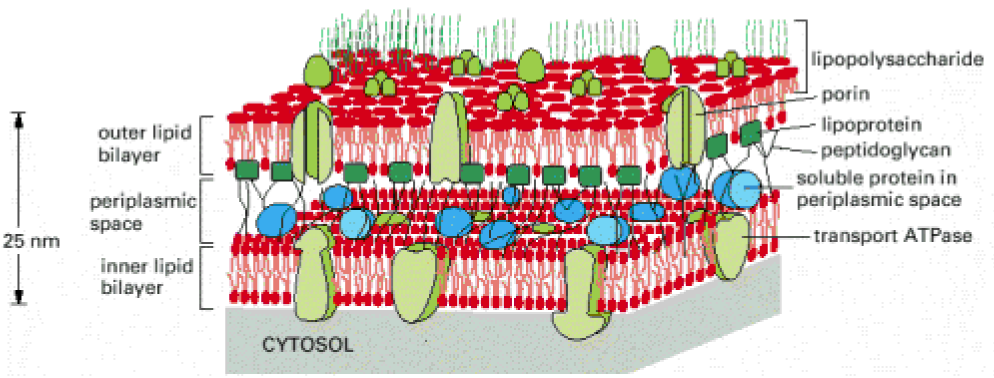


Four major phospholipids in mammalian plasma membranes. Note that different head groups are represented by different colors. All the lipid molecules shown are derived from glycerol except for sphingomyelin, which is derived from serine.
http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=mboc4.figgrp.1879

The *fatty acid tails* typically are linear alkanes, for example, $CH_3(CH_2)_{15}$-, which is called "palmitoyl." The name of the lipid is determined by the type of headgroup and the type of tails it has. For example, dipalmitoylphosphatidylcholine has the phosphatidylcholine headgroup and two palmitoyl tails.

General Structure of Lipids and Phospholipids

The lipid bilayer is essential for cell structure, but the cell wall can be a very complex structure, especially in prokaryotes, such as *E. coli*, shown below:



A small section of the double membrane of an *E. coli* bacterium. The inner membrane is the cell's plasma membrane. Between the inner and outer lipid bilayer membranes is a highly porous, rigid peptidoglycan, composed of protein and polysaccharide, that constitutes the bacterial cell wall. It is attached to lipoprotein molecules in the outer membrane and fills the *periplasmic space* (only a little of the peptidoglycan is shown). This space also contains a variety of soluble protein molecules. The dashed threads (shown in *green)* at the top represent the polysaccharide chains of the special lipopolysaccharide molecules that form the external monolayer of the outer membrane; for clarity, only a few of these chains are shown. Bacteria with double membranes are called *Gram-negative* because they do not retain the dark blue dye used in Gram staining. Bacteria with single membranes (but thicker cell walls), such as staphylococci and streptococci, retain the blue dye and therefore are called *Gram-positive;* their single membrane is analogous to the inner (plasma) membrane of Gram-negative bacteria. http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=mboc4.figgrp.2023